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DOCUMENT NUMBER:

128:214161

TITLE:

Screening assay for identification of agents which

alter expression of parathyroid hormone-related

protein in mammalian cells

INVENTOR(S):

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E.

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Wolfgang E.

SOURCE:

PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PAT	PATENT NO.				ND	DATE		APPLICATION NO.						DATE			
							19980226		WO 1997-US14836 19970822									
	WO						19980827											
		W:	ΑL,	AM,	ΑT,	ΑU,	ΑZ,	ΒA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
			DK,	EE,	ES,	FI,	GB,	GE,	GH,	HU,	IL,	IS,	JP,	KE,	KG,	ΚP,	KR,	ΚZ,
			LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	ΝZ,	PL,
															TT,			
											KZ,							
		RW:													DK,	ES,	FI,	FR,
			GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,
			-	-			SN,											
	US 5914233			A 19990622			US 1997-915868						19970821					
	AU 9741587			A1 19980306			AU 1997-41587						1997	0822				
US 2002061509 A1						1	2002	0523		τ	S 20	01-8	7944	5	2001	0611		
PRIORITY APPLN. INFO.:															1996			
										US 1	997-	9158	68	Α	1997	0821		
										wo 1	997-	US14	836	W	1997	0822		
										US 1	999-	2836	75	В3	1999	0401		

A cell-based assay technique for identifying and evaluating chem. compds. AΒ and agents which affect the prodn. of parathyroid hormone-related protein (Pth-rP) in mammalian cells and other cell types is set forth. Specifically , tumor cell lines are transformed with an expression vector comprising a DNA sequence encoding a promoter region of PTH-rP operatively linked to a reporter gene encoding an assayable product and cultured under conditions which permit expression of the assayable product. Chem. agent and factors can then be identified by their ability to modulate the expression of the reporter gene, thereby affecting the prodn. of the assayable product. Such agents are then tested for inhibitory effects on tumor cell growth and for stimulatory effects on bone formation and repair. A chimeric gene comprising Pth-rP promoter linked to the firefly luciferase gene was prepd. This chimeric reporter gene was expressed in human breast cancer cell line MDA-MD-231 and human lung cancer cell line RWGT2. 6-Thioguanine and 5-benzylidene hydrazino-1,2,3,4-tetrazole were found to inhibit reporter gene expression. Both compds. lowered serum calcium and Pth-rP levels when administered to mice with squamous cell carcinoma of the lung. A similar assay indicated that acriflavinium hydrochloride stimulated expression of Pth-rP promoter-driven reporter genes.

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TT
     204278-43-3
     RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
        (nucleotide sequence; screening assay for identification of agents
        which alter expression of parathyroid hormone-related protein in
       mammalian cells)
     204278-43-3 HCAPLUS
RN
     DNA (human humoral hypercalcemic factor gene promoter region) (9CI) (CA
CN
     INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     9001-45-0, .beta.-Glucuronidase 9001-78-9
     9031-11-2, .beta.-Galactosidase 9040-07-7,
     Chloramphenicol acetyltransferase 12629-01-5, Somatotropin
     (human) 61970-00-1, Luciferase
     RL: ARU (Analytical role, unclassified); ANST (Analytical study)
        (parathyroid hormone-related protein gene promoter fused to gene for;
        screening assay for identification of agents which alter expression of
        parathyroid hormone-related protein in mammalian cells)
     9001-45-0 HCAPLUS
RN
     Glucuronidase, .beta. - (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     9001-78-9 HCAPLUS
RN
     Phosphatase, alkaline (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     9031-11-2 HCAPLUS
RN
     Galactosidase, .beta.- (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     9040-07-7 HCAPLUS
RN
    Acetyltransferase, chloramphenicol (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     12629-01-5 HCAPLUS
RN
     Somatotropin (human) (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     61970-00-1 HCAPLUS
RN
     Luciferase (firefly luciferin) (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     103370-86-1, Humoral hypercalcemic factor
IT
     RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
        (screening assay for identification of agents which alter expression of
        parathyroid hormone-related protein in mammalian cells)
     103370-86-1 HCAPLUS
RN
     Humoral hypercalcemic factor (9CI)
                                        (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     86-40-8 154-42-7, 6-Thioguanine 10444-59-4
ΙT
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
        (screening assay for identification of agents which alter expression of
        parathyroid hormone-related protein in mammalian cells)
RN
     86-40-8 HCAPLUS
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CN Acridinium, 3,6-diamino-10-methyl-, chloride (8CI, 9CI) (CA INDEX NAME)

• c1-

RN 154-42-7 HCAPLUS CN 6H-Purine-6-thione, 2-amino-1,7-dihydro- (9CI) (CA INDEX NAME)

RN 10444-59-4 HCAPLUS CN Benzaldehyde, 1H-tetrazol-5-ylhydrazone (9CI) (CA INDEX NAME)

$$N-N=CH-Ph$$